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REMARKS

Reconsideration of this application is respectfully requested.

Claims 2-24 and 245-279 were previously pending in this application. Claims 2-24 have been canceled. Claims 245, 246, 250, 251, 252, 253, 259, 260, 261, 262, 275, 277 and 279 have been amended above. No claims have been added. Accordingly, claims 245-279 as amended are presented for further examination.

The first page (line 1) of the specification has been amended by inserting information cross-referencing this divisional application with the prior parent application, Serial No. 08/574,443, filed on December 15, 1995. The parent application was revived for purposes of continuity so that the present divisional application could be filed.

Several informalities in the specification have been corrected. These include changes on pages 9, 64, 81, 105, 109, 114, 123, 127, 134, 151, 159, 180 and 181, none of which is believed to have inserted new matter into Applicants' disclosure. Referring to the aforementioned page 81 (line 7), Applicants have corrected the description of an incompatible cell to mean "a cell *incapable* of processing RNA by removal of the processing element." The definition of an incompatible cell is in contrast to the definition of a compatible cell that precedes it. In the preceding lines on page 81, a compatible cell is defined as "a cell capable of processing RNA by removal of the processing element." See page 81, lines 5-6. In clarifying the definition of an incompatible cell, Applicants have corrected an obvious error in the specification that is clear from its context. Thus, no new matter has been inserted thereby. The issue of a "compatible cell" and "substantially removed" is discussed further below in the section dealing with the indefiniteness rejection under 35 U.S.C. §112, second paragraph.

For the sake of clarity and definiteness, relatively minor changes have been made to twelve claims above. The inadvertent period in claim 245 has been replaced with a colon. In claim 246, the phrase "polymer or oligomer"

has been replaced with -- polymeric interactions --, thereby providing a proper antecedent basis in the claim for the latter. In claim 262, the second occurrence of "polycationic" [interactions] has been replaced with -- polyanionic -- . In a similar way, the term "polyionic" [polymer] in line 3 of claim 275 has been changed to -- polyanionic -- . Furthermore, the word "complex" in the second line of claim 279 has been changed to the past participle, i.e., complexed. It is believed that the foregoing changes to claims 245, 246, 262, 275 and 279 either meet the Examiner's requirements or adopt her suggestions for claim clarity.

Minor changes have also been made to claims 250, 251, 252, 253, 259, 260, 261, 275 and 277. All of these minor changes affect only the Markush language in the foregoing claims. It is believed that the amended claim language in these claims conforms to the accepted proper usage under U.S. patent practice.

Entry of the above amendments to the specification and claims is respectfully requested.

Objection to Patent Drawings

Acknowledgement is made of the Notice of Draftperson's Patent Drawings Review that was issued in connection with this application. Formal drawings will be submitted as soon as allowable subject matter has been indicated in this application.

Submission of Sequence Listing

Applicants are filing concurrently with this Amendment a response to the Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

The Rejection for Double Patenting Under 35 U.S.C. §101

Claims 2-24 stand provisionally rejected under 35 U.S.C. §101 as claiming the same invention as that of claims 2-24 of copending Application Nos.: 08/978,632, 08/978,633, 08/978,635, 8/978,636, 08/978,637, 08/978,638 ,08/978,639, and O8/574,443. As indicated by the Examiner on page 2 of the February 17, 1999 Office Action, "This is a provisional double patenting rejection since the conflicting claims have not in fact been patented."

As indicated above, claims 2-24 have now been canceled as they should have been when claims 245-302 were presented in Applicants' November 25, 1997 Preliminary Amendment. Any inconvenience caused by this oversight is sincerely regretted.

In view of the cancelation of claims 2-24, Applicants respectfully request withdrawal of the double patenting rejection

The Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 2-21, 245-246, 262, and 279 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the Office Action (page 3), the Examiner stated:

> Claims 2-21 are indefinite because they depend from canceled claim 1. Therefore, claims 2-21 do not depend on any indefinite claim.
>
> Claim 245 is indefinite for location of a period in the claim after the word "attached."
>
> There is no antecedent basis in claim 246 for the language "the polymer or oligomer."
>
> Claim 262 is drawn to the same element "polycationic interactions or polycationic interactions" and is redundant.
>
> It appears from the language of claim 279 that the word "complex" should be in the past tense.

The Examiner's comments above have been well taken, leading to claims 245, 246, 262 and 279 having been amended and claims 2-24 having been canceled (see the opening remarks of this Amendment).

In light of the cancelation of claims 2-24 and the above amendments to claims 245, 246, 262 and 279, it is respectfully requested that the rejection under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

The Rejection Under 35 U.S.C. §112, First Paragraph

Claims 2-21 and 245-279 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In the Office Action (pages 3-5), the Examiner stated:

> The constructs taught in the claims 2-24 are broadly drawn to a multitude of possible nucleic acid based constructs for use in a cell to produce a product (and in any context, *in vivo* or *in vitro),* comprising: (1) the construct as linear or circular, (2) the construct as comprising 1,2 or 3 strands, (3) comprising a terminus, a polynucleotide tail which can hybridize, (4) composed of RNA or DNA or combinations, (5)containing chemically modified nucleotides or analogs, (6) containing non-nucleic acid entities composed of polymers or ligands or a combination, (7) further specifying the natural and synthetic polymers, the synthetic homo- or heteropolymer with a net charge, (8)the construct imparting a "further biological activity" by the modified nucleotide, analog, entity, ligand or combination of those, further defined as nuclease resistance, cell recognition, cell binding, and cellular or nuclear localization or a combination, (9) a ligand attached to one of the modified nucleotides, etc. of claim1, further described as attached to a "segment" or "tail" of the construct , and further defined as being a macromolecule or small molecule or combination. Claims 22-24 describe a second construct "which when present in a cell produces a product, said construct being bound non-ionically to an entity comprising a chemical modification or a ligand."
>
> Claims 245-266 are drawn to a composition of a multimeric complex of more than one monomeric unit attached: (a) to each other through polymeric interactions, or (b) to a binding matrix through polymeric interactions, or both. Dependent claims are drawn to (1) linear or branched polymer or oligomers, homopolymer or

heteropolymer, (2) an analyte-specific moiety, capable of recognizing a component in a biological system, being: a virus, phage, bacterium, cell or cellular material, tissue, organ or organism, or combination, or from a protein (antibody, hormone, growth factor, lymphokine or cytokine and a cellular matrix protein or a combination), polysaccharide, fatty acid, fatty acid ester and a polynucleotide (linear or circular and single stranded) or a combination (3)a naturally occurring compound, a modified natural compound, synthetic compound and a recombinantly produced compound, or combination, (4) linear or branched binding matrix selected from a naturally occurring compound, a modified natural compound, a synthetic compound and a recombinantly produced compound or a combination, also selected from a polypeptide, a polynucleotide and a polysaccharide, or a combination, (5) polymeric interactions selected from ionic, H-bonding, dipole-dipole, or a combination, (6) an entity attached to the binding matrix, being a ligand or compound which increases the binding of the binding matrix.

Claims 275-279 are further drawn to a multimeric composition having more than one unit attached to a charged polymer selected from: a polycationic polymer, a polyionic polymer, a polynucleotide, a modified polynucleotide and analog, or a combination. The composition is further limited to a protein component being and antibody or the F(ab')2 fragment, where the antibody is further completed with a target comprising an enzyme.

The Examiner's comments continued on pages 5-8 where she stated:

Claims 267-274 are drawn to a process for delivering a cell effector to a cell comprising providing the multimeric complex of claim 245 (where the multimeric unit is the cell effector) and administration (claims 267-270) and a process for delivering a gene or gene fragment to a cell comprising providing the multimeric complex of claim 245 (where the multimeric unit is the gene or fragment) and administration.

The specification teaches several constructs designed for entry into a cell and expression of one or more sequences to perform a biological function such as antisense inhibition of a nucleic acid. Specifically, several CHENAC constructs are taught prophetically, and pictured in figures 1-13 as vector based constructs constructed by using modified nucleic acid regions and designed to provide improved entry into a cell by way of improved construct-cell interaction. A second group of nucleic acid fused with antibody based constructs are taught prophetically and shown in figures 14-21. Preparation of multimeric insulin by means of nucleic acid hybridization is further taught prophetically and shown in figures 22-23. No exemplification for such constructs is taught in the specification as filed.

Furthermore, vectors ultimately designed for antisense inhibition of HIV in cells by co-expression of antisense DNA under control of a T7 promoter with a T7 polymerase, (represented in figures 24-49) are taught and supported by *in vitro* data. Specifically, construction of the M13 phage vectors pRT-A, pRT-B, and pRT-c are taught which contain the coding sequence for the T7 RNA polymerase driven by the RSV promoter and with an SV40 intron sequence that will be spliced out to

form a functional polymerase enzyme and each respective construct also having the antisense A, B, and C sequences driven by a T7 promoter and terminated by a T7 terminator. A modified version of the pINT-3 construct (the parent vector of pRT-A, B and C vectors before insertion of the antisense sequences) is taught where a polylinker is inserted behind the poly-A tail of the T7 polymerase gene for subsequent sub-cloning of the lacZ gene in this instance to form pINT-LacZ. The result upon introduction in a eukaryotic cell would be synthesis of the T7 polymerase from the RSV promoter which in turn acts upon the T7 promoter to synthesize B-galactosidase.

Furthermore, plasmids are taught containing anti-sense segments introduced into the transcript region of the U1 gene, plasmid pHSD-4 U1 so that upon expression of the transcript, the antisense RNA sequence is produced to the complementary region of the HIV genome. Specifically, pDU1-A, B, C and D were made using the antisense A, B, and C sequences previously described and D as a control containing a non-HIV sequence. A multi-cassette version of the constructs was also made by sub-cloning in tandem the A,B, and C antisense to make pNDU1 (A,B,C) (N meaning the construct was also contained the gene for neomycin resistance).

Other multi-cassette constructs taught were:

(1) TRI 101, an M13 phage vector containing the "A" antisense T7 operon, the "B" antisense T7 operon and the "C" antisense T7 operon in a single construct (figure 46). Co-transfection would be required for expression of the antisense molecules from this construct with a vector that expresses T7 RNA polymerase (suggested is the intron containing construct of example 19); and,

(2) an M13 construct constructed from a multi-ligation of portions of pINT-3 (containing the intron containing polymerase) and the T7 promoter driven A, B, and C sequences (see figure 47).

The specification teaches application of some of these constructs ("various U1 constructs described above" p. 167, last line) in antisense inhibition of HIV in infected U937 cell culture. Specifically the following is shown: (1) expression of A, B, and C antisense by hybridization analysis after expression of the "U1 clone" (p. 169, line 3), (2) expression of the "triple U1 construct' (p. 169, para. (c), line 1) which result in a decrease in p24 production next to the control, and increased % reduction in p24 over time and after re-infection of cells, and these results were confirmed by absence p24 amplification next to control cells via PCR of the targeted DNA, and (3) expression of the construct of figure 50, a fusion product antisense A upstream of B-gal gene where antisense activity of the A portion caused inhibition of B-gal activity as shown in lacZ assays. The results in figure 51 show HIV A/Anti-A activity and HIV A/Anti-ABC (when the triple U1 construct was used by *co-transfection)* as the equivalent of the uninfected cells whereas the infected and control containing cells showed high B-gal expression. Therefore, it does not appear in the specification as filed that the multicassette A,B,C and T7 polymerase construct (expressed on same plasmid) was applied to the same HIV challenge experiments.

Additional constructs are more prophetically taught: the primary nucleic acid construct that propagates production centers for the production of single-stranded antisense, etc. in examples 21-25, and

the retrovirus vector containing sequences for the expression of antisense RNA directed at HIV on page 181, last para.

Continuing on pages 8-11 in the Office Action, the Examiner went on to state:

Claims 22-24 read on any construct bound non-ionically to a ligand or otherwise chemically modified entity, further limited as having a polynucleotide tail terminus and where the tail is hybridized to a complementary polynucleotide sequence. The breadth of genus sought for such is not enabled in view of the lack of specificity of guidance in the specification as filed. The specification fails to provide guidance for the breadth claimed since the claims vaguely claim "constructs" which "produce products." The specification teaches only by way of example HIV inhibition by antisense expression from vector constructs which do not entail chemical modified entities nor polynucleotide termini.

Claims 245-279 are drawn to a "multimeric complex composition" having "monomeric unit(s)" attached via "polymeric interactions." The language "multimeric complex composition" bound via "polymeric interactions" reads on associations of any polymer, ie. any chemical compound or mixture of compounds combined and consisting of essentially repeating structural units, and therefore reads on nylon or any other non-biological polymeric composition as well as duplex DNA, RNA, etc. The scope of the genus sought for such constructs is not enabled in view of the lack of specificity of guidance in the specification as filed. The specification fails to provide guidance for the breadth claimed since the claims nebulously claim "multimeric compositions." The specification teaches only prophetically nucleic acid constructs having multimeric units bound to binding matrices for cell interaction The specification only exemplifies application of constructs for expression of antisense to HIV in which the only "multimeric units" are nucleotides forming duplex DNA "complexes."

Despite the known use in the art of constructs such as nucleic acid vectors having polymeric modifications and conjugated antibodies, etc. for improved cell entry to recombinantly express genes, etc., the broad scope of the instant claims would lead one of ordinary skill in the art to an undue amount of experimentation based on the lack of guidance for making and/or using a representative number of the genus of constructs envisioned by the instant claims as filed.

Furthermore, the claims specify the context for producing the product in a cell and no exemplification of whole organism success is found in the specification as filed. There is a high level of unpredictability in the antisense art and analogous gene therapy art, for *in vivo* (whole organism) applications. The factors considered are analogous to those in the antisense art for successful delivery of such constructs. The barriers include: (1) penetration of the plasma membrane of the target cells to reach the target site in the cytoplasm or nucleus, (2) withstanding enzymatic degradation, and (3) the ability to find and bind the target site and simultaneously avoid non-specific binding (see Branch). Despite the synthesis of more resilient, nuclease

resistant, oligonucleotide backbones and isolated successes with antisense therapy *in vivo,* the majority of designed antisense molecules still face the challenge of successful entry and localization to the intended target and further such that antisense and other effects can routinely be obtained. Note Flanagan et al. who teach "although numerous reports have cited antisense effects using oligonucleotides added to cell medium, direct proof that oligonucleotides enter cells and affect gene inhibition by an antisense mechanism is still lacking (page48, column 1)."

Specifically, *in vitro* results with one antisense molecule are not predictive of *in vivo* (whole organism) success. *In vitro,* antisense specificity to its target may be manipulated by "raising the temperature or changing the ionic strength, manipulations that are commonly used to reduce background binding in nucleic acid hybridization experiments." (Branch, p. 48) Discovery of antisense molecules with "enhanced specificity" *in vivo* requires further experimentation for which no guidance is taught in the specification. Note Branch who teaches the state of the art for designing an antisense which inhibits a target *in vivo:* it "is very difficult to predict what portions of an RNA molecule will be accessible *in vivo,* effective antisense molecules must be found empirically by screening a large number of candidates for their ability to act inside cells (Branch, p.49)." And in the instant case, the claims read broadly on administration of an antisense inhibitor in any cell, therefore the whole organism included. While the specification teaches cell culture inhibition, no evidence of successful *in vivo* (whole organism) antisense inhibition has been shown, nor do the culture examples correlate with whole organism delivery.

One of skill in the art would not accept on its face the successful delivery of the disclosed antisense molecules *in vivo* in view of the lack of guidance in the specification and the unpredictability in the art. Specifically the specification does not teach (1) stability of the antisense molecule *in vivo,* (2)effective delivery to the whole organism and specificity to the target tissues, (3) dosage and toxicity, nor (4) entry of molecule into cell and effective action therein marked by visualization of the desired treatment effects. These key factors are those found to be highly unpredictable in the art as discussed *supra.* The lack of teaching of these factors in inhibition of the target, coupled to the amount of "trial and error" experimentation involved in the deduction of these results would lead one skilled in the art to necessarily practice an undue amount of experimentation *in vivo.*

No determination of enablement can be made for claims 2-21 because there is no independent claim from which they depend. Without knowing what claims 2-21 depend on, the full scope of the claims is not known.

The enablement rejection is respectfully traversed.

With respect to the application of the enablement rejection to claims 2-24, such grounds have been rendered moot, of course, by the cancelation of these claims.

With respect to claims 245-279, it is respectfully submitted that the subject matter of these claims is fully enabling such that a person skilled in the art could practice, without undue experimentation, Applicants' claimed invention. It is respectfully submitted that the ordinarily skilled artisan, armed with the disclosure, could practice the multimeric composition and gene delivery process set forth in Applicants' present invention as claimed.

Reconsideration and withdrawal of the enablement rejection are respectfully requested.

The Rejection Under 35 U.S.C. §112, First Paragraph

Claims 2-24 and 245-266 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the Office Action (pages 12-13), the Examiner stated:

> Claims 2-21 are drawn to a missing independent claim and therefore the scope claimed is not able to be determined. Claims 22-24 are drawn to a broad scope of constructs which are bound non-ionically to an entity having a chemical modification or a ligand and produce a product in a cell. Claims 245-266 are drawn to a "multimeric complex composition" having "monomeric unit(s)" attached via "polymeric interactions."
>
> The claims broadly encompass "constructs" for producing a "product" and it is not clear what is embraced by the claims. The claims read on vectors, genomes, cell processes like translation, transcription, etc. Furthermore, the scope of "chemical modification" as used in claim 22 is not clear in relation to the construct. Claims 245-266 further read on any polymer composition.
>
> The instant specification describes prophetically a number of potential modified nucleic acid constructs for expression of an entity in a cell. The supporting figures provide limited additional disclosure of relevant identifying structural characteristics because they primarily correspond to expression vector based constructs which are only one facet of the invention in light of the nebulous scope claimed.
>
> Clearly the specification only considers vector-like constructs for delivery and expression of nucleic acids. Specifically, for claims 245-

266, the only "multimeric compositions" exemplified are those for antisense inhibition of HIV.

Furthermore, the actual constructs used in the HIV challenge and Lac-Z assays taught in the specification are not described in clear and exact terms (p. 169, line 3 recites "U1 clone"; p. 169, para. © line I recites "triple U1 construct"; and p. 167, last line recites "various U1 constructs described above') and it is not clear whether the constructs used had the intron sequence in the T7 polymerase, or even which constructs were used in the assays.

Despite the known predictability of standard vector construction in the molecular biology art, in view of the nearly infinite scope claimed and the lack of adequate description in the specification for such a broad genus of possible "constructs" and "multimeric compositions" coupled with the high level of unpredictability for constructs which could fall within this genus such as those involving gene therapy, the specification as filed fails to provide one skilled in the art enough description to show possession of a representative number of "construct" or ("multimeric composition" species for the breadth claimed.

See the June 15, 1998 (Vol. 63, No. 114, Pages 32639-32645) Federal Register for the interim guidelines for the examination of patent applications under the 35 U.S.C. 112 "Written Description" requirement.

The written description rejection is respectfully traversed.

With respect to claims 2-24, the cancelation of those claims above renders the instant description rejection moot as it applies to the now canceled claims.

With respect to claims 245-279, it is believed that the scope of these claims is of proper breadth so as to reasonably convey to one skilled in the relevant art that the present inventors had possession at the time this application was first filed in December 1995 of the same matter now being claimed.

Reconsideration and withdrawal of the written description rejection are respectfully requested.

The First Rejection Under 35 U.S.C. §102

Claims 22-24 stand rejected under 35 U.S.C. §102(e) as being anticipated by Meyer et al., U.S. Patent No. 5,574,142, issued on November 12, 1996, based

upon an application filed on December 15, 1992. In the Office Action (page 14), the Examiner stated:

> The claimed invention is drawn to any construct which when present in a cell produces a product, and is bound non-ionically to an entity comprising a modification or a ligand, and further comprises a hybridized polynucleotide tail.
>
> Meyer et al. teach a covalently linked conjugate of an oligonucleotide (ODN) with a peptide and a carrier or targeting ligand (ODN-peptide-carrier) including a therapeutic oligonucleotide which is capable of selectively binding to a target sequence of DNA, RNA or protein inside a target cell. The invention of Meyer et al. Reads on all of the instant claimed limitations for a non-naturally occurring construct for production of a product in a cell (in Meyer, an antisense oligonucleotide is produced).

With the cancelation of claims 2-24 above, it is believed that the anticipation rejection based upon Meyer's patent has been rendered moot.

Reconsideration and withdrawal of this anticipation rejection are respectfully requested.

The Second Rejection Under 35 U.S.C. §102

Claims 245-279 stand rejected under 35 U.S.C. §102(e) as being anticipated by Sullivan, U.S. Patent No. 5,583,020, issued on December 10, 1996. In the Office Action (pages 14-15), the Examiner stated:

> The claimed invention is drawn to any multimeric complex composition bound through polymeric interactions and/or attached to a charged polymer and process of delivery of said multimeric composition to a cell.
>
> Sullivan teaches compositions and methods for improved cell permeability to negatively charged polymers such as RNA and DNA. Specifically, he teaches application of permeability enhancer molecules and ligand-permeability enhancer molecules containing cationic groups which can ion-pair with anionic groups present on the negatively charged polymer.

The anticipation rejection based on Sullivan is respectfully traversed.

Applicants respectfully contend that there is a lack of material identity between their claimed elements and Sullivan's disclosure.

Reconsideration and withdrawal of the rejection is respectfully requested.

The Third Rejection Under 35 U.S.C. §102

Claims 245-279 stand rejected under 35 U.S.C. §102(e) as being anticipated by Curiel et al., U.S. Patent No. 5,521,291, issued on May 28, 1996. In the Office Action (page 15), the Examiner stated:

> The claimed invention is drawn to any multimeric complex composition bound through polymeric interactions and/or attached to a charged polymer and process of delivery of said multimeric composition to a cell.
>
> Curiel et al. teach conjugates in which a virus is bound via an antibody to a substance having an affinity for nucleic acid, for transporting gene constructs into higher eucaryotic cells and pharmaceutical compositions thereof. It is within the scope of the invention to apply F(ab')2 fragments and/or complex said antibody with a target comprising an enzyme.

The anticipation rejection by Curiel et al. is respectfully traversed.

It is respectfully contended that Curiel's patent neither discloses nor suggests Applicants' claimed invention. Reconsideration and withdrawal of this anticipation rejection is respectfully requested.

The Fourth Rejection Under 35 U.S.C. §102

Claims 245-266 and 275 stand rejected under 35 U.S.C. §102(e) as being anticipated by Edwards et al., U.S. Patent No. 5,693,463, issued on December 2, 1997. In the Office Action (page 15), the Examiner stated:

> The claimed invention is drawn to any multimeric complex composition bound through polymeric interactions and/or attached to a charged polymer.

> Edwards et al. teach the design of sequence-specific DNA-binding drugs (and methods of detecting) comprised of homo- or hetero-meric subunits of molecules and the use of said molecules as covalently attached moieties to aid in the binding of nucleic acid or other macromolecular polymers to nucleic acid sequences.

The anticipation rejection by Edwards et al. is respectfully traversed.

It is believed that Edwards' disclosure does not anticipate the present invention.

Reconsideration and withdrawal of the fourth anticipation rejection are respectfully requested.

The Fifth Rejection Under 35 U.S.C. §102

Claims 245 and 275-279 stand rejected under 35 U.S.C. §102(e) as being anticipated by Buechler, et al., U.S. Patent No. 5,480,792, issued on January 2, 1996, based upon an application filed on September 14, 1990. In the Office Action (page 16), the Examiner stated:

> The claimed invention is drawn to any multimeric complex composition bound through polymeric interactions and/or attached to a charged polymer. Specifically in claims 276-279, multimeric compositions comprising protein and/or antibody components.
>
> Buechler et al. teach complexes of ligand-receptor and target-ligands.

The anticipation rejection by Buechler et al. is respectfully traversed.

It is respectfully submitted that Buechler et al. do not teach or suggest Applicants' claimed invention.

Reconsideration and withdrawal of this rejection is respectfully requested.

The Sixth Rejection Under 35 U.S.C. §102

Claims 245-279 stand rejected under 35 U.S.C. §102(e) as being anticipated by Paul et al., U.S. Patent No. 5,736,387, issued on April 7, 1998. In the Office Action (page 16), the Examiner stated:

> The claimed invention is drawn to any multimeric complex composition bound through polymeric interactions and/or attached to a charged polymer and process of delivery of said multimeric composition to a cell.
>
> Paul et al. teach retroviral vectors for directing gene delivery to a specific sub-population of mammalian cells. The vectors having chimeric targeting proteins containing a ligand moiety capable of binding to receptors present on target cells and an uptake moiety promoting entry of the vector into the target cell.

The anticipation rejection by Paul et al. is respectfully traversed.

It is believed that Paul's patent does not anticipate Applicants' invention due to a lack of identity of material elements with the subject matter of the claims at hand.

Reconsideration and withdrawal of the anticipation rejection is respectfully requested.

* * * * * * *

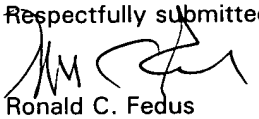
SUMMARY AND CONCLUSIONS

Claims 245-279 are being presented for further examination, with claims 2-24 having been canceled and claims 245, 246, 250, 251, 252, 253, 259, 260, 261, 262, 275, 277 and 279 having been amended above.

This Amendment is being accompanied by a Request For An Extension Of Time (3 months) and authorization for the small entity fee therefor. No other fee or fees are believed due for filing this Amendment. In the event that any other fee or fees are due, however, authorization is hereby given to charge the amount of any such other fee(s) to Deposit Account No. 05-1135, or to credit any overpayment thereto.

If a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney request that he be contacted at the number provided below.

Respectfully submitted,



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